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Palladium-Catalyzed α-Arylation of Aryloxyketones for the Synthesis of 2,3-Disubstituted Benzofurans†

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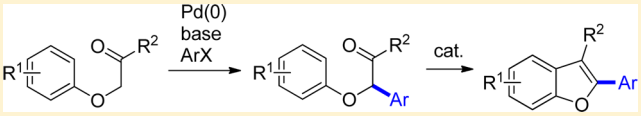
Supporting Information

ABSTRACT: A highly efficient palladium-catalyzed α-arylation of aryloxyketones has been developed, allowing for facile installation of various (hetero)aryl groups at C2 position in good to excellent yields. Subsequent cyclodehydration of the resulting α-arylated aryloxyketones provided rapid access to diverse 2,3-disubstitured benzofurans.



INTRODUCTION

Benzofuran ubiquitously found in various natural products and functional materials constitutes an important class of chemical backbones.[1] As a subclass, 2,3-disubstituted benzofurans embedded in a number of natural products and pharmaceuticals exhibit a broad spectrum of biological activities, prompting development of a number of efficient synthetic strategies for this heterocyle (Figure 1).[2]

2,3-Disubstituted benzofurans, traditionally, have been synthesized by transition metal-catalyzed cross-coupling reactions of prefunctionalized benzofurans such as C2-halogenated[3] or stannylated[4] benzofurans with aryl boronic acids or aryl halides. Guided by powerful C−H activation technologies, direct arylation of 2- or 3-substituted benzofurans with aryl halides have also appeared.[5] More recently, oxidative dehydrogenative cross-coupling approach[6] to install heteroaryl moiety at C2 site of benzofurans was reported, although the scope and yields are still limited. Despite all these advances, development of more direct synthetic methods to access to this skeleton is in high demand. Our recent contribution to this area has resulted in efficient synthetic routes to several 2,3-benzofuran-containing natural products.[7,8]

In both cases, we have employed direct arylation protocol to install aryl group at the C2 position of benzofurans. In one case as illustrated in Scheme 1a, however, we observed dimerized benzofuran product **3** as a byproduct under the direct arylation conditions. Although research to find reaction conditions to minimize the formation of the dimer is plausible with benzofuran **1**, alternatively, we envisioned that introduction of aryl group at C2 site via palladium-catalyzed α-arylation of aryloxyketone[9,10] followed by dehydrative cyclization would give the desired 2,3-disubstituted benzofuran product as a way to avoid this problem (Scheme 1b).

RESULTS AND DISCUSSION

To evaluate this idea, we began our studies with **4a**[11] and 4-bromoanisole as substrates to optimize the reaction conditions for α-arylation (Table 1). Reactions of **4a** (0.236 mmol) were conducted with 4-bromoanisole (2.5 equiv), $Pd(OAc)_2$ (4 mol %), phosphine ligand (8 mol %), and NaH (1.1 equiv) in THF (3 mL) at 120 °C. Screening of suitable phosphine ligand for this transformation revealed that SPhos gave the best isolated yield of the desired product **5a** (entries 1−8). Other bases such as NaO*t*-Bu or KO*t*-Bu furnished the inferior results (entries 9 and 10). Replacement of THF by toluene decreased the chemical yield (entry 11). While reactions at 100 °C provided comparable results, lowering the reaction temperature to 80 °C led to incomplete conversion and decreased yield (entries 12 and 13). Likewise, reducing the amount of 4-bromoanisole resulted in incomplete conversion and lower chemical yields (entries 14 and 15). Use of 1.3 equiv of NaH rather gave unsatisfactory results (entry 16). Use of 4-iodoanisole yielded the product in 38% yield although yield improvement was observed at 80 °C (entry 17).

Having found optimal conditions for α-arylation of aryloxyketones, we reacted **4a** with several aryl bromides under optimized conditions as shown in Scheme 2. Not only electron-rich aryl groups but also electron-poor aryl groups were introduced in good yields. Heterocycle such as pyridine can be incorporated to afford **5n** in 42% yield.

Substrate scope of this reaction was further investigated by exposing other aryloxyketones with several aryl bromides under optimized conditions. The results are shown in Scheme 3. Various functional groups attached to aryloxyketones seemed compatible under these reaction conditions. Substrates containing methoxyl, phenyl, fluoro, or chloro groups underwent smooth α-arylation to give the corresponding products in good to excellent yields. Aryloxyketone bearing a methoxycarbonyl group at R^1 site reacted with 4-bromoanisole and ethyl 4-bromobenzoate to afford **5ac** and **5ad**, respectively (entries 13 and 14). Substrates possessing multiple substituents at R^1 and R^2 positions (**4i**−**4k**) were also allowed to react with several aryl bromides to furnish the desired products, **5aj**−**5ao**

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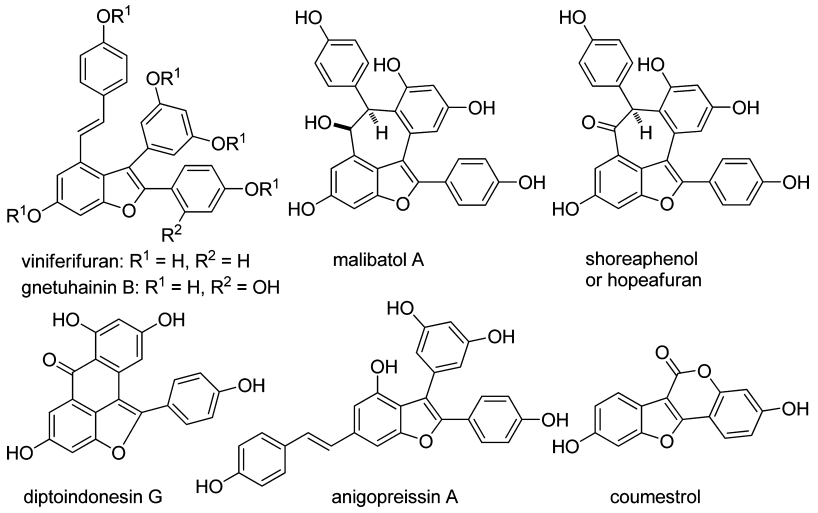
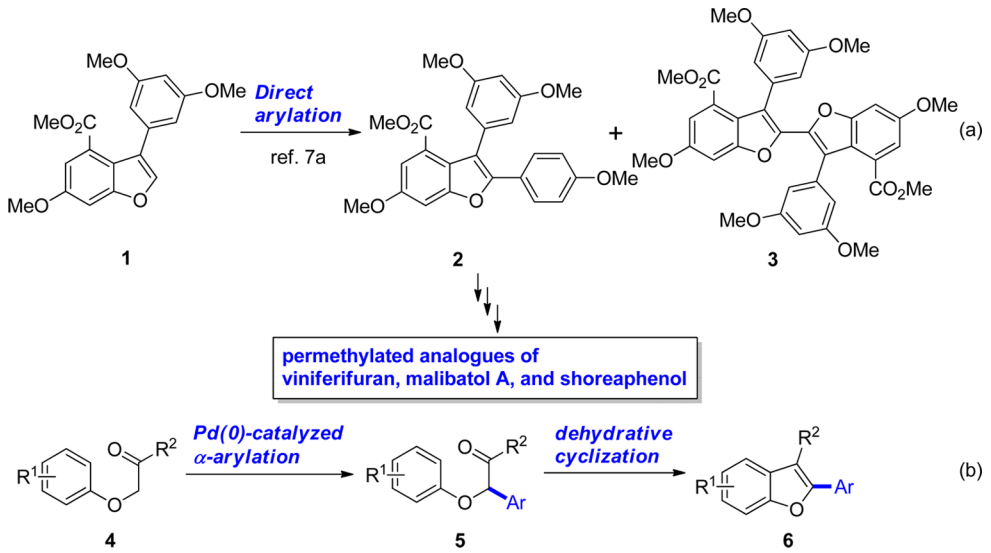


Figure 1. Some natural products having a 2,3-disubstituted benzofuran unit.

Scheme 1. Novel Approach to 2,3-Disubstituted Benzofurans



(entries 20−25). Larger scale experiments were conducted with several substrates to produce the corresponding α-arylated compounds in good yields (entries 2, 5, 6, 21, 24, and 25).

Finally, cyclodehydration of the resulting 2-arylated aryloxyketones was attempted (Scheme 4).[12] Several different reaction conditions were screened for cyclization. Dehydrative cyclization of **5** under the influence of catalytic amounts of PTSA provided the corresponding benzofurans in good yields (**7**, **9**, **10**, **13**−**16**). In some cases, more than stoichiometric amounts of catalyst were required for efficient conversion (**6**, **8**, and **12**).[13] Upon exposure to PPTS (0.1 equiv) in refluxing toluene to trigger cyclization,[14] **5aj** was transformed to 2,3-diarylbenzofuran **2**, previously employed as an important intermediate for the syntheses of permethylated analogues of viniferifuran, malibatol A, and shoreaphenol as well as diptoindonesin G.[7] In cases of **5v** and **5aa**, use of $Bi(OTf)_3$ gave better isolation yields of the desired products (**8** and **11**).[15]

In summary, we have successfully employed palladium-catalyzed α-arylation as a means to install a variety of aryl groups at the C2 position of aryloxyketones. Subsequent cyclization of the resulting adducts afforded 2,3-disubstituted benzofurans in high yields. In particular, efficiency of this protocol was further demonstrated by facile and effective construction of a key intermediate utilized previously en route to several natural products bearing a 2,3-disubstituted benzofuran unit. Extension of this method for the synthesis of other heterocycles is currently in progress.

■ EXPERIMENTAL SECTION

General Methods. Unless specified, all reagents and starting materials were purchased from commercial sources and used as received without purification. "Concentrated" refers to the removal of volatile solvents via distillation using a rotary evaporator. "Dried" refers to pouring onto, or passing through, anhydrous magnesium sulfate followed by filtration. Flash chromatography was performed using silica gel (230−400 mesh) with hexanes, ethyl acetate, and dichloromethane as eluent. All reactions were monitored by thin-layer chromatography on 0.25 mm silica plates (F-254) visualizing with UV light. ^{1}H and ^{13}C NMR spectra were recorded on 400 MHz NMR spectrometer and were described as chemical shifts, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet), coupling constant in hertz (Hz), and number of protons. IR spectra were recorded on FT-IR using diamond ATR technique and were described

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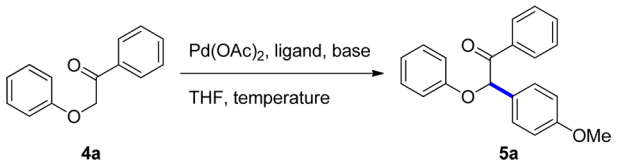
Table 1. Reaction Optimization[a]



4a 5a

entry	ligand	base	solvent	temperature (°C)	yield (%)[b]
1	PPh_3	NaH	THF	120	33
2	BINAP	NaH	THF	120	30
3	Xantphos	NaH	THF	120	67
4	XPhos	NaH	THF	120	76
5	*t*-BuXPhos	NaH	THF	120	53
6	JohnPhos	NaH	THF	120	46
7	RuPhos	NaH	THF	120	99
8	SPhos	NaH	THF	120	99.5
9	SPhos	NaO*t*-Bu	THF	120	37
10	SPhos	KO*t*-Bu	THF	120	59
11	SPhos	NaH	toluene	120	80
12	SPhos	NaH	THF	100	92−95
13	SPhos	NaH	THF	80	60
14[c]	SPhos	NaH	THF	120	94
15[d]	SPhos	NaH	THF	120	87
16[e]	SPhos	NaH	THF	120	84
17[f]	SPhos	NaH	THF	120	38, 50[g]

[a]A mixture of **4a** (0.236 mmol), 4-bromoanisole (2.5 equiv), $Pd(OAc)_2$ (4 mol %), phosphine ligand (8 mol %), and base (1.1 equiv) in solvent (3 mL) was heated at 120 °C for 2 h unless otherwise noted. [b]Isolated yield (%) [c]4-Bromoanisole (2.0 equiv) was used. [d]4-Bromoanisole (1.5 equiv) was used. [e]NaH (1.3 equiv) was used. [f]4-Iodoanisole was used. [g]Reaction conducted at 80 °C.

as wavenumbers (cm^{-1}). HRMS were measured with electrospray ionization (ESI) and Q-TOF mass analyzer.

General Procedure for the Synthesis of 4.[16] A mixture of appropriate 2-bromoacetophenone (2.512 mmol), phenol (1.25 equiv), and K_2CO_3 (1.5 equiv) in acetone (8.0 mL) was stirred at 80 °C for 2 h. The reaction mixture was concentrated under reduced pressure to give the crude residue which was diluted with ethyl acetate and washed with water. The water layer was extracted with ethyl acetate two more times. The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo to give a crude mixture which was purified by silica gel column chromatography (hexane:ethyl acetate:dichloromethane) to afford **4**.

*2-Phenoxy-1-phenylethanone (**4a**).* White solid: mp 72.6−73.3 °C (lit. 72.5−73.0 °C)[17] (490.8 mg, 92%); IR (ATR) ν = 3065, 1703, 1596, 1497, 1447, 1386, 1300, 1223 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 7.6 Hz, 2H), 7.62 (t, J = 7.6 Hz, 1H), 7.50 (t, J = 7.6 Hz, 2H), 7.29 (t, J = 7.6 Hz, 2H), 6.99 (t, J = 7.2 Hz, 1H), 6.95 (d, J = 8.0 Hz, 2H), 5.28 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.7, 158.1, 134.7, 134.0, 129.7, 129.0, 128.3, 121.8, 114.9, 70.9; HRMS (ESI-QTOF) calcd for $[C_{14}H_{13}O_2]^+$ m/z 213.0910, found 213.0913.

*2-(4-Methoxyphenoxy)-1-(4-methoxyphenyl)ethanone (**4b**).* Pale brown solid: mp 67.2−69.4 °C (622.5 mg, 91%); IR (ATR) ν = 3065, 3008, 2842, 1695, 1599, 1505, 1450, 1384, 1318, 1262, 1224 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 9.2 Hz, 2H), 6.96 (d, J = 8.8 Hz, 2H), 6.89 (d, J = 9.2 Hz, 2H), 6.82 (d, J = 9.2 Hz, 2H), 5.16 (s, 2H), 3.88 (s, 3H), 3.76 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.6, 164.1, 154.5, 152.4, 130.7, 127.8, 116.1, 114.8, 114.1, 71.8, 55.8, 55.7; HRMS (ESI-QTOF) calcd for $[C_{16}H_{17}O_4]^+$ m/z 273.1121, found 273.1121.

*2-(3-Methoxyphenoxy)-1-(4-methoxyphenyl)ethanone (**4c**).* Pale brown solid: mp 48.1−49.5 °C (608.8 mg, 89%); IR (ATR) ν = 3008, 2959, 2836, 1692, 1591, 1490, 1454, 1433, 1309, 1263, 1231 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 8.8 Hz, 2H), 7.18 (t, J = 7.6 Hz, 1H), 6.96 (d, J = 8.8 Hz, 2H), 6.55−6.51 (m, 3H), 5.20 (s, 2H), 3.88 (s, 3H), 3.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.1, 164.2, 161.0, 159.4, 130.7, 130.1, 127.8, 114.2, 107.4, 106.8, 101.6, 70.8, 55.7, 55.5; HRMS (ESI-QTOF) calcd for $[C_{16}H_{17}O_4]^+$ m/z 273.1121, found 273.1128.

*2-([1,1′-Biphenyl]-4-yloxy)-1-(4-methoxyphenyl)ethanone (**4d**).* White solid: mp 123.5−124.2 °C (695.8 mg, 87%); IR (ATR) ν = 3353, 3037, 2969, 2910, 2842, 1682, 1594, 1510, 1485, 1457, 1367, 1298, 1263, 1227 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 8.0 Hz, 2H), 7.53 (d, J = 8.0 Hz, 2H), 7.51 (d, J = 8.0 Hz, 2H), 7.41 (t, J = 8.0 Hz, 2H), 7.30 (t, J = 7.6 Hz, 1H), 7.01 (d, J = 8.0 Hz, 2H), 6.97 (d, J = 8.0 Hz, 2H), 5.26 (s, 2H), 3.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.2, 164.2, 157.8, 140.8, 134.8, 130.7, 128.9, 128.4, 127.8, 126.9, 115.2, 114.2, 71.0, 55.7; HRMS (ESI-QTOF) calcd for $[C_{21}H_{19}O_4]^+$ m/z 319.1329, found 319.1327.

*2-(4-Chlorophenoxy)-1-phenylethanone (**4e**).* White solid: mp 92.2−94.4 °C (lit. 95−97 °C)[18] (433.8 mg, 70%); IR (ATR) ν = 3375, 3062, 2901, 2851, 1693, 1580, 1487, 1434, 1285, 1208 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, J = 7.6 Hz, 2H), 7.63 (t, J = 7.2 Hz, 1H), 7.51 (t, J = 7.6 Hz, 2H), 7.24 (d, J = 9.2 Hz, 2H), 6.87 (d, J = 8.8 Hz, 2H), 5.27 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ194.2, 156.8, 134.5, 134.2, 129.6, 129.0, 128.2, 126.7, 116.3, 71.1; HRMS (Q-TOF) calcd for $[C_{14}H_{12}ClO_2]^+$ m/z 247.0520, found 247.0519.

*2-(4-(tert-Butyl)phenoxy)-1-phenylethanone (**4f**).* White solid: mp 67.3−68.2 °C (lit. 67−68 °C)[19] (357.3 mg, 53%); IR (ATR) ν = 3390, 2957, 2900, 1702, 1609, 1512, 1434, 1414, 1289, 1226 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 7.6 Hz, 2H), 7.62 (t, J = 7.6 Hz, 1H), 7.50 (t, J = 7.6 Hz, 2H), 7.30 (d, J = 8.8 Hz, 2H), 6.88 (d, J = 9.2 Hz, 2H), 5.25 (s, 2H), 1.29 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.9, 155.9, 144.5, 134.8, 134.0, 129.0, 128.3, 126.5, 114.4, 71.1, 34.3, 31.6; HRMS (ESI-QTOF) calcd for $[C_{18}H_{21}O_2]^+$ m/z 269.1536, found 269.1533.

*Methyl 3-(2-oxo-2-phenylethoxy)benzoate (**4g**).* Pale brown solid: mp 117.5−118.0 °C (448.1 mg, 66%); IR (ATR) ν = 3406, 2900, 2843, 1703, 1582, 1486, 1428, 1289, 1209 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 7.2 Hz, 2H), 7.68 (d, J = 7.6 Hz, 1H), 7.64 (t, J = 6.8 Hz, 1H), 7.59 (s, 1H), 7.52 (t, J = 7.6 Hz, 2H), 7.37 (t, J = 8.0 Hz, 1H), 7.19 (dd, J = 2.8, 8.4 Hz, 1H), 5.35 (s, 2H), 3.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.0, 166.9, 158.1, 134.6, 134.2, 131.7, 129.8, 129.1, 128.2, 123.1, 120.4, 115.0, 70.8, 52.4; HRMS (ESI-QTOF) calcd for $[C_{16}H_{17}O_4]^+$ m/z 271.0965, found 271.0965.

*1-(4-Fluorophenyl)-2-phenoxyethanone (**4h**).* White solid: mp 88.6−89.5 °C (416.4 mg, 71%); IR (ATR) ν = 3066, 2901, 2846, 1701, 1588, 1495, 1431, 1299, 1222 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.06 (dd, J = 5.6, 8.8 Hz, 2H), 7.29 (t, J = 8.8 Hz, 2H), 7.17 (t, J = 8.8 Hz, 2H), 6.99 (t, J = 7.2 Hz, 1H), 6.95 (d, J = 8.8 Hz, 2H), 5.21 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.5, 166.3 (d, J_{CF} = 254.6 Hz), 158.0, 131.2 (d, J_{CF} = 9.4 Hz), 129.8, 121.9, 116.3, 116.1, 114.9, 71.1; HRMS (ESI-QTOF) calcd for $[C_{14}H_{12}FO_2]^+$ m/z 231.0816, found 231.0824.

*Methyl 3-(2-(3,5-dimethoxyphenyl)-2-oxoethoxy)-5-methoxybenzoate (**4i**).*[7a] White solid: mp 105.4−106.9 °C (869.0 mg, 96%); IR (ATR) ν = 3093, 2947, 2898, 2841, 1721, 1591, 1437, 1323, 1296, 1235 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.23 (dd, J = 1.2, 2.0 Hz, 1H), 7.19 (dd, J = 1.2, 2.0 Hz, 1H), 7.11 (d, J = 2.0 Hz, 2H), 7.38 (t, J = 2.0 Hz, 1H), 6.70 (t, J = 2.0 Hz, 1H), 5.28 (s, 2H), 3.90 (s, 3H), 3.85 (s, 6H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.5, 166.8, 161.2, 160.8, 159.1, 136.3, 132.3, 108.5, 107.6, 106.8, 106.2, 105.9, 70.8, 55.8, 55.79, 52.4; HRMS (ESI-QTOF) calcd for $[C_{19}H_{21}O_7]^+$ m/z 361.1282, found 361.1274.

*2-(3,4-Dimethoxyphenoxy)-1-phenylethanone (**4j**).* White solid: mp 78.3−78.9 °C (649.8 mg, 95%); IR (ATR) ν = 3379, 2941, 2836, 1699, 1593, 1508, 1440, 1304, 1263, 1225 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 7.2 Hz, 2H), 7.62 (t, J = 7.6 Hz, 1H), 7.51 (t, J = 7.6 Hz, 2H), 6.75 (d, J = 8.8 Hz, 1H), 6.65 (d, J = 2.8 Hz, 1H), 6.39 (dd, J = 2.8, 8.8 Hz, 1H), 5.23 (s, 2H), 3.85 (s, 3H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.8, 152.8, 150.1, 144.3, 134.8, 134.0, 129.0, 128.3, 111.7, 104.0, 101.7, 71.6, 56.5, 56.0; HRMS (ESI-QTOF) calcd for $[C_{16}H_{17}O_4]^+$ m/z 273.1121, found 273.1119.

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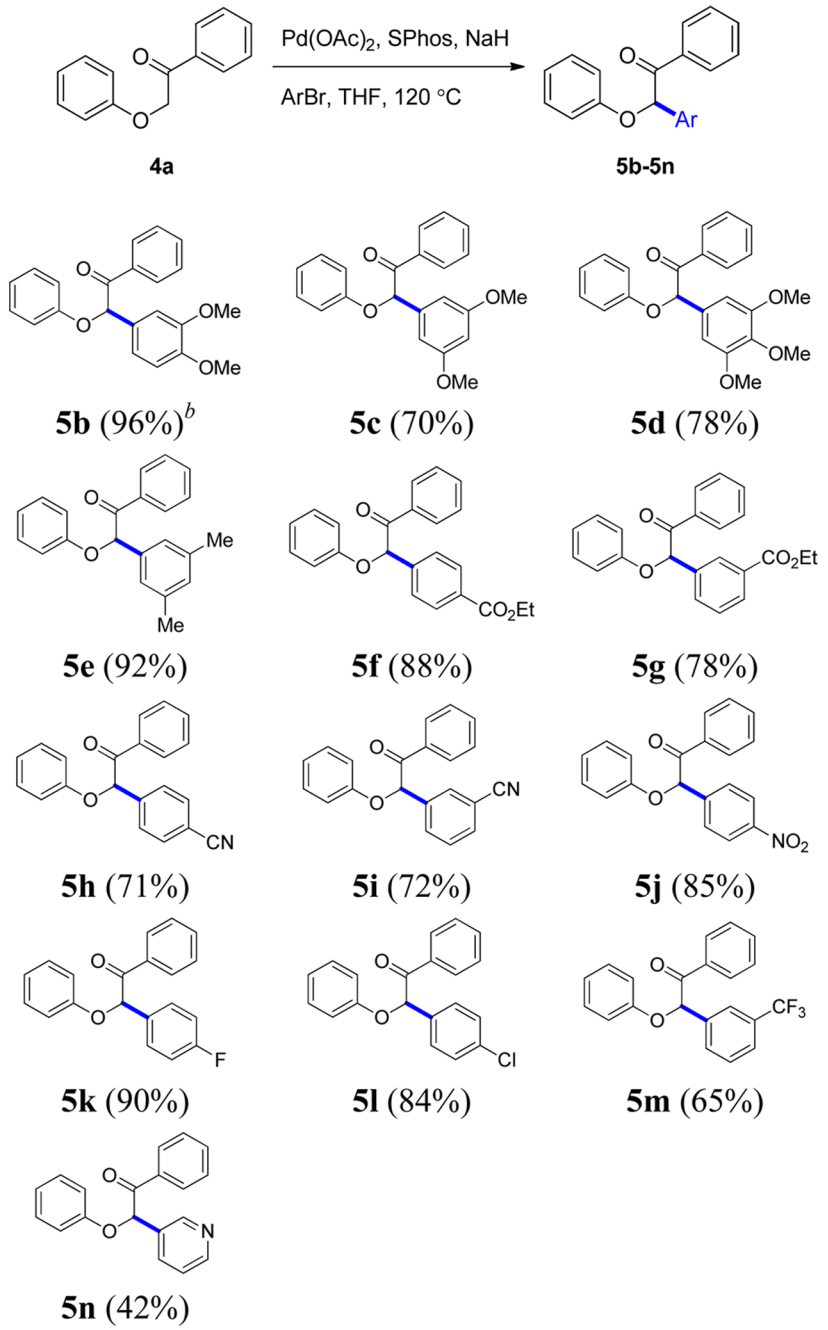
Scheme 2. α-Arylation of 4a with Aryl Bromides[a]



[a]A mixture of **4a** (0.236 mmol), ArBr (2.5 equiv), $Pd(OAc)_2$ (4 mol %), SPhos (8 mol %), and NaH (1.1 equiv) in THF (3 mL) was heated at 120 °C for 2 h unless otherwise noted. [b]Isolated yields (%) are in parentheses.

*2-(3,5-Dimethoxyphenoxy)-1-(3-methoxyphenyl)ethanone (**4k**).* White solid: mp 92.1−93.5 °C (1137.9 mg, 77%); IR (ATR) ν = 3403, 2898, 2839, 1711, 1598, 1476, 1429, 1262, 1192 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, J = 7.6 Hz, 1H), 7.51 (s, 1H), 7.40 (t, J = 8.0 Hz, 1H), 7.16 (dd, J = 2.4, 8.0 Hz, 1H), 6.13−6.11 (m, 3H), 5.22 (s, 2H), 3.87 (s, 3H), 3.76 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.0, 161.7, 160.1, 160.0, 136.0, 130.0, 120.6, 120.56, 112.5, 93.9, 70.9, 55.7, 55.5; HRMS (ESI-QTOF) calcd for $[C_{17}H_{19}O_5]^+$ m/z 303.1227, found 303.1226.

General Procedure for the Synthesis of 5. A mixture of aryloxyketone **4** (0.236 mmol), aryl bromide (2.5 equiv), palladium acetate (4 mol %), and SPhos (8 mol %) in THF (3.0 mL) was added 60% NaH (1.1 equiv) at rt. The reaction mixture was sealed in a 7 mL vial and heated at 120 °C for 2 h. The reaction mixture was quenched with water and concentrated under reduced pressure to give the crude residue which was diluted with ethyl acetate and washed with water. The water layer was extracted with ethyl acetate two more times. The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo to give a crude mixture which was purified by silica gel column chromatography (hexane:ethyl acetate:dichloromethane) to afford **5**.

*2-(4-Methoxyphenyl)-2-phenoxy-1-phenylethanone (**5a**).* Colorless oil (74.8 mg, 99.5%): IR (ATR) ν = 3060, 2936, 1694, 1594, 1519, 1490, 1447, 1344, 1214 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, J = 8.0 Hz, 2H), 7.53 (t, J = 7.6 Hz, 1H), 7.48 (d, J = 8.4 Hz, 2H), 7.41 (t, J = 7.6 Hz, 2H), 7.23 (t, J = 7.6 Hz, 2H), 6.96−6.89 (m, 5H) 6.35 (s, 1H), 3.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.0, 160.1, 157.7, 134.8, 133.6, 129.7, 129.3, 129.2, 128.8, 127.4, 121.8, 115.8,

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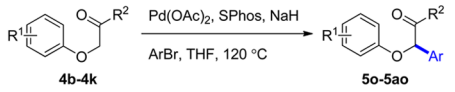
Scheme 3. α-Arylation of 4b−4k with Aryl Bromides[a]



entry	4	5	yield (%)[b]
1	4b	5o	68
2[c]	4b	5p	87
3	4c	5q	64
4	4d	5r	81
5[c]	4d	5s	88
6[c]	4e	5v	83
7	4e	5w	42
8	4f	5x	89
9	4f	5y	86
10	4f	5z	84
11	4f	5aa	91
12	4f	5ab	92
13	4g	5ac	60
14	4g	5ad	85
15	4h	5ae	85
16	4h	5af	93
17	4h	5ag	79
18	4h	5ah	87
19	4h	5ai	90
20	4i	5aj	84
21[c]	4i	5ak	72
22	4j	5al	81
23	4j	5am	65
24[c]	4k	5an	73
25[c]	4k	5ao	65

[a]A mixture of **4** (0.236 mmol), ArBr (2.5 equiv), $Pd(OAc)_2$ (4 mol %), SPhos (8 mol %), and NaH (1.1 equiv) in THF (3 mL) was heated at 120 °C for 2 h unless otherwise noted. [b]Isolated yields (%). [c]0.708 mmol of **4** was used

114.6, 82.3, 55.4; HRMS (ESI-QTOF) calcd for $[C_{21}H_{19}O_3]^+$ m/z 319.1329, found 319.1325.

*2-(3,4-Dimethoxyphenyl)-2-phenoxy-1-phenylethanone (**5b**).* Colorless oil (78.9 mg, 96%): IR (ATR) ν = 2934, 1692, 1594, 1512, 1461, 1340 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 7.6 Hz, 2H), 7.54 (t, J = 7.6 Hz, 1H), 7.42 (t, J = 7.2 Hz, 2H), 7.24−7.23 (m, 2H), 7.11 (d, J = 8.0 Hz, 1H), 7.06 (s, 1H), 6.97−6.94 (m, 3H), 6.86 (d, J = 7.6 Hz, 1H), 6.34 (s, 1H) 3.87 (s, 3H), 3.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.9, 157.7, 149.6, 149.5, 134.8, 133.6, 129.7, 129.2, 128.7, 127.7, 121.8, 120.6, 115.8, 111.3, 110.4, 82.4, 56.1, 56.0; HRMS (ESI-QTOF) calcd for $[C_{22}H_{21}O_4]^+$ m/z 349.1434, found 349.1433.

*2-(3,5-Dimethoxyphenyl)-2-phenoxy-1-phenylethanone (**5c**).* Colorless oil (57.6 mg, 70%): IR (ATR) ν = 3060, 2934, 1694, 1592, 1491, 1456, 1428, 1348, 1287, 1204, 1153 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 8.0 Hz, 2H), 7.53 (t, J = 7.6 Hz, 1H), 7.41 (t, J = 7.6 Hz, 2H), 7.24−7.22 (m, 2H), 6.97−6.94 (m, 3H), 6.72 (s, 2H), 6.41 (s, 1H), 6.25 (s, 1H), 3.77 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.0, 161.3, 157.6, 137.7, 134.6, 133.7, 129.7, 129.5, 128.7, 121.9, 115.8, 105.4, 100.7, 83.0, 55.6; HRMS (ESI-QTOF) calcd for $[C_{22}H_{21}O_4]^+$ m/z 349.1434, found 349.1430.

*2-Phenoxy-1-phenyl-2-(3,4,5-trimethoxyphenyl)ethanone (**5d**).* White gum (69.7 mg, 78%): IR (ATR) ν = 3062, 2936, 1680, 1589, 1494, 1450, 1421, 1334, 1273, 1219, 1119 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 8.0 Hz, 2H), 7.56 (t, J = 7.6 Hz, 1H), 7.44 (t, J = 7.6 Hz, 2H), 7.28−7.24 (m, 2H), 6.99−6.94 (m, 3H), 6.77 (s, 2H), 6.28 (s, 1H), 3.84 (s, 6H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.3, 153.8, 133.8, 129.8, 129.3, 128.8, 122.0, 115.8, 104.6, 82.9,

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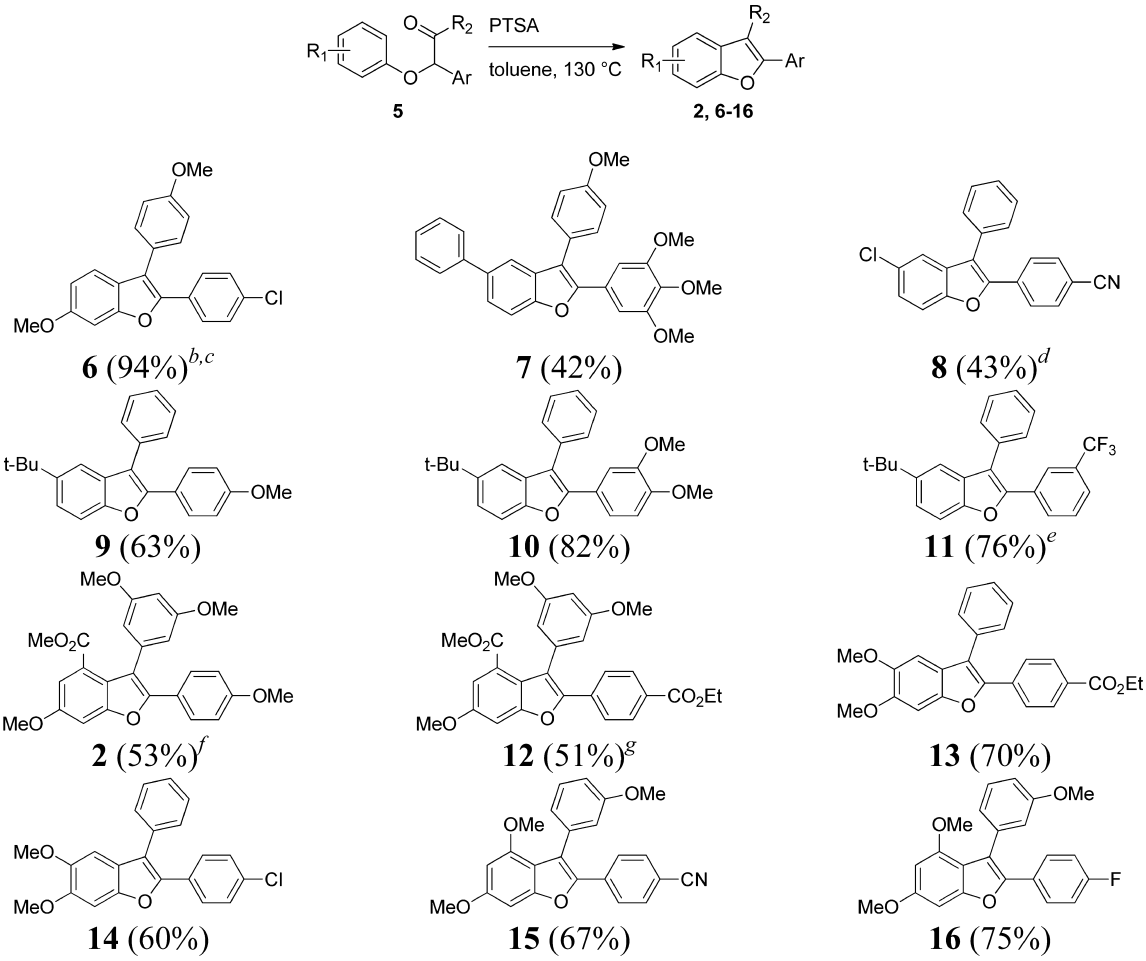
Scheme 4. Dehydrative Cyclization of 5 to Benzofurans[a]



[a]A solution of **5** (0.1 mmol) in the presence of PTSA (0.1 equiv) in toluene (3 mL) was heated at 130 °C unless otherwise noted. [b]Isolated yields (%) are in parentheses. [c]PTSA (1 equiv) was used. [d]$Bi(OTf)_3$ (2 equiv) was used in CH_2Cl_2 at 100 °C. [e]$Bi(OTf)_3$ (0.2 equiv) was used in toluene at 90 °C. [f]PPTS (0.1 equiv) was used in toluene. [g]PTSA (2 equiv) was used.

56.4; HRMS (ESI-QTOF) calcd for $[C_{23}H_{23}O_5]^+$ *m*/*z* 379.1540, found 379.1542.

*2-(3,5-Dimethylphenyl)-2-phenoxy-1-phenylethanone (**5e**).* White solid: mp 115.5−117.8 °C (68.7 mg, 92%); IR (ATR) ν = 3053, 2918, 1685, 1584, 1483 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.4 Hz, 2H), 7.52 (t, *J* = 7.6 Hz, 1H), 7.41 (t, *J* = 7.6 Hz, 2H), 7.25−7.22 (m, 2H), 7.18 (s, 2H), 6.96−6.92 (m, 4H), 6.30 (s, 1H), 2.30 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.1, 157.8, 138.8, 135.2, 134.7, 133.6, 130.7, 129.7, 129.4, 128.7, 125.4, 121.7, 115.7, 82.9, 21.5; HRMS (ESI-QTOF) calcd for $[C_{22}H_{21}O_2]^+$ *m*/*z* 317.1536, found 317.1535.

*Ethyl 4-(2-oxo-1-phenoxy-2-phenylethyl)benzoate (**5f**).* Colorless oil (74.8 mg, 88%): IR (ATR) ν = 3061, 2980, 1703, 1698, 1594, 1491, 1447, 1413, 1366, 1273, 1219, 1103 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.4 Hz, 2H), 8.03 (d, *J* = 8.0 Hz, 2H), 7.67 (d, *J* = 8.4 Hz, 2H), 7.54 (t, *J* = 7.2 Hz, 1H), 7.41 (t, *J* = 7.6 Hz, 2H), 7.27−7.24 (m, 2H), 6.99−6.95 (m, 3H), 6.36 (s, 1H), 4.36, (q, *J* = 7.2 Hz, 2H), 1.37 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.8, 166.2, 140.4, 134.4, 133.0, 130.9, 130.3, 129.8, 129.5, 128.8, 127.1, 122.2, 115.8, 82.9, 61.3, 14.5; HRMS (ESI-QTOF) calcd for $[C_{23}H_{21}O_4]^+$ *m*/*z* 361.1434, found 361.1437.

*Ethyl 3-(2-oxo-1-phenoxy-2-phenylethyl)benzoate (**5g**).* Colorless oil (66.3 mg, 78%): IR (ATR) ν = 3062, 2981, 1716, 1707, 1594, 1491, 1446, 1369, 1281, 1218, 1186 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.27 (s, 1H), 8.05−8.01 (m, 3H), 7.77 (d, *J* = 8.0 Hz, 1H), 7.54 (t, *J* = 7.6 Hz, 1H) 7.49−7.40 (m, 3H), 7.27−7.24 (m, 2H), 6.99−6.95 (m, 3H), 6.40 (s, 1H), 4.38 (q, *J* = 6.8 Hz, 2H), 1.39 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ193.2, 157.5, 146.5, 136.1, 133.9, 131.7, 131.4, 130.0, 129.8, 129.4, 129.2, 128.8, 128.6, 122.1, 115.8, 82.5, 61.4, 14.5; HRMS (ESI-QTOF) calcd for $[C_{23}H_{21}O_4]^+$ *m*/*z* 361.1434, found 361.1435.

*4-(2-Oxo-1-phenoxy-2-phenylethyl)benzonitrile (**5h**).* Brown gum (52.5 mg, 71%): IR (ATR) ν = 3061, 2924, 2228, 1694, 1593, 1491, 1447, 1410, 1217 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 7.6 Hz, 2H), 7.71 (d, *J* = 8.0 Hz, 2H), 7.67 (d, *J* = 8.0 Hz, 2H), 7.55 (t, *J* = 7.2 Hz, 1H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.28−7.24 (m, 2H), 6.99 (t, *J* = 7.6 Hz, 1H), 6.94 (d, *J* = 8.0 Hz, 2H), 6.35 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ195.4, 157.0, 140.8, 134.1, 132.8, 129.9, 129.5, 128.9, 127.7, 122.4, 118.5, 115.6, 112.7, 82.4; HRMS (ESI-QTOF) calcd for $[C_{21}H_{16}NO_2]^+$ *m*/*z* 314.1176, found 314.1178.

*3-(2-Oxo-1-phenoxy-2-phenylethyl)benzonitrile (**5i**).* White solid: mp 83.1−86.1 °C (53.2 mg, 72%); IR (ATR) ν = 3061, 2230, 1692, 1593, 1489, 1211 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.4 Hz, 2H), 7.92 (s, 1H), 7.81 (d, *J* = 7.6 Hz, 1H), 7.63 (d, *J* = 7.6 Hz, 1H), 7.57 (t, *J* = 7.6 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 1H), 7.44 (t, *J* = 7.6 Hz, 2H), 7.29−7.25 (m, 2H), 6.99 (t, *J* = 7.2 Hz, 1H), 6.94 (d, *J* = 8.4 Hz, 2H), 6.33 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.5, 157.0, 137.3, 134.2, 134.1, 132.4, 131.5, 130.7, 130.0, 129.9, 129.5, 128.9, 122.5, 118.5, 115.6, 113.3, 82.0; HRMS (ESI-QTOF) calcd for $[C_{21}H_{16}NO_2]^+$ *m*/*z* 314.1176, found 314.1179.

*2-(4-Nitrophenyl)-2-phenoxy-1-phenylethanone (**5j**).* Brown oil (66.9 mg, 85%): IR (ATR) ν = 3069, 2925, 1698, 1587, 1543, 1492, 1445, 1361, 1211 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J* = 8.4 Hz, 2H), 8.02 (d, *J* = 8.0 Hz, 2H), 7.78 (d, *J* = 8.8 Hz, 2H), 7.56 (t,

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J = 7.6 Hz, 1H), 7.43 (t, J = 7.6 Hz, 2H), 7.29−7.25 (m, 2H), 7.00 (t, J = 7.6 Hz, 1H), 6.95 (d, J = 8.8 Hz, 2H), 6.39 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.3, 157.0, 148.1, 142.8, 134.2, 134.1, 130.0, 129.5, 128.9, 127.9, 124.2, 122.5, 115.7, 82.3; HRMS (ESI-QTOF) calcd for $[C_{20}H_{16}NO_4]^+$ m/z 334.1074, found 334.1069.

2-(4-Fluorophenyl)-2-phenoxy-1-phenylethanone (**5k**). White solid: mp 91.4−92.9 °C (65.1 mg, 90%); IR (ATR) ν = 3071, 2923, 1688, 1590, 1492, 1448, 1361, 1298, 1259, 1218 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 8.0 Hz, 2H), 7.56−7.52 (m, 3H) 7.41 (t, J = 7.6 Hz, 2H), 7.26−7.22 (m, 2H), 7.07 (t, J = 7.6 Hz, 2H), 6.98−6.92 (m, 3H), 6.34 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.9, 163.0 (d, J_{CF} = 246.7 Hz), 157.5, 134.5, 133.8, 131.3 (d, J_{CF} = 3.3 Hz), 129.8, 129.4 (d, J_{CF} = 8.3 Hz), 129.3, 128.8, 122.0, 116.1 (d, J_{CF} = 21.7 Hz), 115.7, 82.1; HRMS (ESI-QTOF) calcd for $[C_{20}H_{16}FO_2]^+$ m/z 307.1129, found 307.1121.

2-(4-Chlorophenyl)-2-phenoxy-1-phenylethanone (**5l**). White solid: mp 107.1−110.6 °C (64.0 mg, 84%); IR (ATR) ν = 3061, 1694, 1594, 1489, 1447, 1218 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 7.6 Hz, 2H), 7.55−7.50 (m, 3H), 7.41 (t, J = 7.6 Hz, 2H), 7.35 (d, J = 8.0 Hz, 2H), 7.26−7.23 (m, 2H), 6.98−6.92 (m, 3H), 6.31 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.8, 157.4, 134.8, 134.4, 134.1, 133.9, 129.8, 129.4, 129.3, 128.8, 128.7, 122.1, 115.7, 82.2; HRMS (ESI-QTOF) calcd for $[C_{20}H_{16}ClO_2]^+$ m/z 323.0833, found 323.0832.

2-Phenoxy-1-phenyl-2-(3-(trifluoromethyl)phenyl)ethanone (**5m**). White solid: mp 79.6−81.4 °C (54.7 mg, 65%); IR (ATR) ν = 3063, 2923, 1682, 1594, 1492, 1447, 1326, 1215, 1162, 1121 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, J = 7.6 Hz, 2H), 7.88 (s, 1H), 7.76 (d, J = 7.6 Hz, 1H), 7.59 (d, J = 8.0 Hz, 1H), 7.56−7.48 (m, 2H), 7.42 (t, J = 7.6 Hz, 2H), 7.27−7.24 (m, 2H), 6.99−6.95 (m, 3H), 6.37 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ195.8, 157.3, 136.7, 134.3, 134.0, 131.5 (d, J_{CF} = 32.1 Hz), 130.5, 129.9, 129.6, 129.4, 128.9, 125.7 (q, J_{CF} = 3.6 Hz), 124.1 (q, J_{CF} = 3.8 Hz), 122.3, 115.7, 82.4; HRMS (ESI-QTOF) calcd for $[C_{21}H_{16}F_3O_2]^+$ m/z 357.1097, found 357.1099.

2-Phenoxy-1-phenyl-2-(pyridin-3-yl)ethanone (**5n**). Brown oil (28.7 mg, 42%): IR (ATR) ν = 3062, 2923, 1739, 1687, 1590, 1488, 1449, 1419, 1269, 1190 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.85 (s, 1H), 8.60 (d, J = 4.8 Hz, 1H), 8.04 (d, J = 8.0 Hz, 2H), 7.89 (d, J = 8.0 Hz, 1H), 7.56 (t, J = 7.6 Hz, 1H), 7.43 (t, J = 7.6 Hz, 2H), 7.32 (dd, J = 4.8, 8.0 Hz, 1H), 7.28−7.24 (m, 2H), 7.00−6.94 (m, 3H), 6.41 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.4, 157.2, 150.1, 148.9, 135.1, 134.3, 134.1, 131.5, 129.9, 129.3, 128.9, 124.0, 122.3, 115.7, 80.6; HRMS (ESI-QTOF) calcd for $[C_{19}H_{16}NO_2]^+$ m/z 290.1176, found 290.1173.

2-(4-Methoxyphenoxy)-1,2-bis(4-methoxyphenyl)ethanone (**5o**). Colorless oil (60.7 mg, 68%): IR (ATR) ν = 3002, 2933, 1681, 1596, 1503, 1460, 1359, 1305, 1212, 1167 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 8.8 Hz, 2H), 7.46 (d, J = 8.4 Hz, 2H), 6.90−6.86 (m, 6H), 6.76 (d, J = 9.2 Hz, 2H), 6.19 (s, 1H), 3.82 (s, 3H), 3.77 (s, 3H), 3.72 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.9, 163.8, 159.9, 154.5, 151.9, 131.7, 128.9, 128.1, 127.7, 117.1, 114.7, 114.5, 113.9, 83.3, 55.7, 55.6, 55.4; HRMS (ESI-QTOF) calcd for $[C_{23}H_{23}O_5]^+$ m/z 379.1540, found 379.1545.

2-(4-Methoxyphenoxy)-1-(4-methoxyphenyl)-2-(3,4,5-trimethoxyphenyl)ethanone (**5p**). White gum (270.1 mg, 87%): IR (ATR) ν = 3067, 2934, 1671, 1593, 1502, 1459, 1421, 1331, 1219, 1178, 1120 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, J = 8.8 Hz, 2H), 6.91−6.88 (m, 4H), 6.79−6.77 (m, 4H), 6.13 (s, 1H), 3.84 (s, 9H), 3.82 (s, 3H), 3.73 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.7, 163.9, 154.6, 153.7, 151.8, 138.2, 131.8, 131.5, 127.6, 117.0, 114.8, 113.9, 104.4, 83.9, 60.9, 56.3, 55.7, 55.6; HRMS (ESI-QTOF) calcd for $[C_{25}H_{27}O_7]^+$ m/z 439.1751, found 439.1756.

2-(4-Chlorophenyl)-2-(3-methoxyphenoxy)-1-(4-methoxyphenyl)ethanone (**5q**). White gum (57.8 mg, 64%): IR (ATR) ν = 3069, 2932, 1683, 1593, 1488, 1453, 1255, 1197 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, J = 8.8 Hz, 2H), 7.51 (d, J = 8.0 Hz, 2H), 7.34 (d, J = 8.0 Hz, 2H), 7.12 (t, J = 8.4 Hz, 1H), 6.88 (d, J = 8.4 Hz, 2H), 6.53−6.50 (m, 3H), 6.25 (s, 1H), 3.83 (s, 3H), 3.74 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.1, 164.1, 161.0, 158.7, 134.7, 134.4, 131.8, 130.2, 129.2, 128.6, 127.2, 114.1, 107.7, 107.4, 102.2, 82.1, 55.6, 55.4; HRMS (ESI-QTOF) calcd for $[C_{22}H_{20}ClO_4]^+$ m/z 383.1045, found 383.1042.

2-([1,1′-Biphenyl]-4-yloxy)-1,2-bis(4-methoxyphenyl)ethanone (**5r**). Yellow gum (81.1 mg, 81%): IR (ATR) ν = 3193, 2923, 2837, 1681, 1596, 1510, 1484, 1458, 1420, 1362, 1305, 1227, 1166 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 9.2 Hz, 2H), 7.51−7.45 (m, 6H), 7.39 (t, J = 7.6 Hz, 2H), 7.30 (d, J = 7.2 Hz, 1H), 7.00 (d, J = 8.4 Hz, 2H), 6.92 (d, J = 7.2 Hz, 2H), 6.90 (d, J = 8.8 Hz, 2H), 6.33 (s, 1H), 3.84 (s, 3H), 3.79 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.5, 163.9, 160.1, 157.4, 151.9, 140.8, 134.7, 131.8, 129.0, 128.8, 128.4, 127.8, 127.6, 126.9, 116.0, 114.6, 114.0, 82.4, 55.6, 55.4; HRMS (ESI-QTOF) calcd for $[C_{28}H_{25}O_4]^+$ m/z 425.1747, found 425.1746.

2-([1,1′-Biphenyl]-4-yloxy)-1-(4-methoxyphenyl)-2-(3,4,5-trimethoxyphenyl)ethanone (**5s**). Colorless oil (301.9 mg, 88%): IR (ATR) ν = 3002, 2936, 1683, 1594, 1507, 1485, 1459, 1419, 1330, 1262, 1229, 1170, 1125 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, J = 8.0 Hz, 2H), 7.52−7.47 (m, 4H), 7.40 (t, J = 7.6 Hz, 2H), 7.29 (t, J = 7.2 Hz, 1H), 7.02 (d, J = 8.4 Hz, 2H), 6.92 (d, J = 8.4 Hz, 2H), 6.80 (s, 2H), 6.27 (s, 1H), 3.86 (s, 6H), 3.85 (s, 3H), 3.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.3, 164.1, 157.3, 153.8, 140.7, 138.4, 134.9, 131.8, 131.1, 128.9, 128.4, 127.5, 127.0, 126.9, 116.0, 114.1, 104.6, 82.9, 61.0, 56.4, 55.6; HRMS (ESI-QTOF) calcd for $[C_{30}H_{29}O_6]^+$ m/z 485.1959, found 485.1963.

2-(4-Chlorophenoxy)-2-(4-methoxyphenyl)-1-phenylethanone (**5t**). Yellow gum (55.8 mg, 67%): IR (ATR) ν = 3061, 2956, 1691, 1594, 1510, 1486, 1446, 1359, 1224, 1173 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 7.6 Hz, 2H), 7.53 (t, J = 7.6 Hz, 1H), 7.46−7.40 (m, 4H), 7.18 (d, J = 8.8 Hz, 2H), 6.90 (d, J = 8.4 Hz, 2H), 6.85 (d, J = 8.4 Hz, 2H), 6.31 (s, 1H), 3.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.5, 160.2, 156.3, 134.6, 133.8, 129.6, 129.2, 128.8, 126.9, 126.7, 117.2, 114.7, 82.5, 55.4; HRMS (ESI-QTOF) calcd for $[C_{21}H_{18}ClO_3]^+$ m/z 353.0939, found 353.0941.

2-(4-Chlorophenoxy)-2-(3,4-dimethoxyphenyl)-1-phenylethanone (**5u**). Yellow oil (56.9 mg, 63%): IR (ATR) ν = 3059, 2933, 1691, 1593, 1512, 1487, 1462, 1419, 1259, 1226 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$); δ 8.01 (d, J = 8.0 Hz, 2H), 7.55 (t, J = 7.6 Hz, 1H), 7.43 (t, J = 7.6 Hz, 2H), 7.19 (d, J = 8.8 Hz, 2H), 7.09 (d, J = 8.4 Hz, 1H), 7.02 (s, 1H), 6.88−6.85 (m, 3H), 6.30 (s, 1H), 3.86 (s, 3H), 3.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.5, 156.3, 149.8, 149.6, 134.7, 133.8, 129.6, 129.2, 128.8, 127.2, 126.8, 120.8, 117.2, 111.4, 110.4, 82.7, 56.1, 56.0; HRMS (ESI-QTOF) calcd for $[C_{22}H_{20}ClO_4]^+$ m/z 383.1045, found 383.1046.

4-(1-(4-Chlorophenoxy)-2-oxo-2-phenylethyl)benzonitrile (**5v**). Colorless gum (204.4 mg, 83%): IR (ATR) ν = 3062, 2923, 2227, 1688, 1589, 1487, 1440, 1420, 1269, 1190 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, J = 7.6 Hz, 2H), 7.69 (s, 4H), 7.57 (t, J = 7.6 Hz, 1H), 7.43 (t, J = 7.6 Hz, 2H), 7.21 (d, J = 8.8 Hz, 2H), 6.87 (d, J = 7.2 Hz, 2H), 6.30 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.0, 155.6, 140.3, 134.3, 134.0, 132.9, 129.9, 129.4, 129.0, 127.7, 127.5, 118.4, 117.0, 112.9, 82.6; HRMS (ESI-QTOF) calcd for $[C_{21}H_{15}ClNO_2]^+$ m/z 348.0786, found 348.0788.

Ethyl 4-(1-(4-Chlorophenoxy)-2-oxo-2-phenylethyl)benzoate (**5w**). Yellowish gum (39.1 mg, 42%): IR (ATR) ν = 3063, 2979, 1702, 1697, 1595, 1486, 1446, 1413, 1366, 1273, 1226 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, J = 8.0 Hz, 2H), 8.00 (d, J = 7.6 Hz, 2H), 7.64 (d, J = 8.0 Hz, 2H), 7.54 (t, J = 7.6 Hz, 1H), 7.41 (d, J = 7.6 Hz, 2H), 7.20 (d, J = 8.4 Hz, 2H), 6.88 (d, J = 8.4 Hz, 2H), 6.33 (s, 1H), 4.36 (q, J = 7.2 Hz, 2H), 1.37 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.3, 166.1, 155.9, 139.8, 134.2, 134.1, 131.1, 130.4, 129.7, 129.4, 128.9, 127.2, 117.1, 83.0, 61.3, 14.5; HRMS (ESI-QTOF) calcd for $[C_{23}H_{20}ClO_4]^+$ m/z 395.1045, found 395.1049.

2-(4-(tert-Butyl)phenoxy)-2-(4-methoxyphenyl)-1-phenylethanone (**5x**). White solid: mp 119.2−119.5 °C (78.7 mg, 89%); IR (ATR) ν = 3069, 2959, 1686, 1606, 1509, 1443, 1360, 1304, 1232, 1184 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, J = 8.0 Hz, 2H), 7.51 (t, J = 8.4 Hz, 1H), 7.47 (d, J = 8.8 Hz, 2H), 7.40 (t, J = 7.6 Hz, 2H), 7.24 (d, J = 8.8 Hz, 2H), 6.89 (d, J = 8.8 Hz, 2H), 6.86 (d, J = 8.8 Hz, 2H), 6.31 (s, 1H), 3.76 (s, 3H), 1.25 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.2, 160.0, 155.5, 144.3, 134.8, 133.6, 129.3, 129.1,

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128.7, 127.6, 126.5, 115.1, 114.5, 82.3, 55.4, 34.2, 31.6; HRMS (ESI-QTOF) calcd for $[C_{25}H_{27}O_3]^+$ m/z 375.1955, found 375.1956.

*2-(4-(tert-Butyl)phenoxy)-2-(3,4-dimethoxyphenyl)-1-phenylethanone (**5y**).* White solid: mp 123.2−124.2 °C (82.1 mg, 86%); IR (ATR) ν = 3057, 2965, 1681, 1590, 1509, 1459, 1416, 1366, 1258, 1233 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 8.0 Hz, 2H), 7.53 (t, J = 7.2 Hz, 1H), 7.41 (t, J = 7.6 Hz, 2H), 7.25 (d, J = 8.4 Hz, 2H), 7.10 (d, J = 8.0 Hz, 1H), 7.05 (s, 1H), 6.88−6.84 (m, 3H), 6.30 (s, 1H), 3.86 (s, 3H), 3.85 (s, 3H), 1.26 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.2, 155.5, 149.5, 144.4, 134.8, 133.6, 129.3, 128.7, 127.9, 126.5, 120.6, 115.2, 111.3, 110.4, 82.5, 56.1, 56.0, 34.2, 31.6; HRMS (ESI-QTOF) calcd for $[C_{26}H_{29}O_4]^+$ m/z 405.2060, found 405.2061.

*Ethyl 4-(1-(4-(tert-butyl)phenoxy)-2-oxo-2-phenylethyl)benzoate (**5z**).* Colorless gum (82.6 mg, 84%): IR (ATR) ν = 3059, 2959, 1715, 1706, 1607, 1509, 1447, 1412, 1364, 1272, 1230 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 8.0 Hz, 2H), 8.03 (d, J = 8.4 Hz, 2H), 7.66 (d, J = 8.0 Hz, 2H), 7.52 (t, J = 7.6 Hz, 1H), 7.40 (t, J = 7.2 Hz, 2H), 7.25 (d, J = 8.0 Hz, 2H), 6.88 (d, J = 8.4 Hz, 2H), 6.33 (s, 1H), 4.35 (q, J = 7.2 Hz, 2H), 1.36 (t, J = 7.2 Hz, 3H), 1.26 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.0, 166.2, 155.2, 144.8, 140.6, 134.4, 133.8, 130.8, 130.2, 129.5, 128.8, 127.1, 126.6, 115.1, 82.9, 61.2, 34.2, 31.6, 14.4; HRMS (ESI-QTOF) calcd for $[C_{27}H_{29}O_4]^+$ m/z 417.2060, found 417.2056.

*2-(4-(tert-Butyl)phenoxy)-1-phenyl-2-(3-(trifluoromethyl)phenyl)-ethanone (**5aa**).* White solid: mp 100.1−100.8 °C (88.6 mg, 91%); IR (ATR) ν = 3070, 2962, 1685, 1597, 1510, 1449, 1364, 1327, 1217 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 7.6 Hz, 2H), 7.87 (s, 1H), 7.75 (d, J = 7.6 Hz, 1H), 7.58 (d, J = 8.0 Hz, 1H), 7.55−7.47 (m, 2H), 7.41 (t, J = 7.6 Hz, 2H), 7.26 (d, J = 8.4 Hz, 2H), 6.89 (d, J = 8.4 Hz, 2H), 6.34 (s, 1H), 1.26 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.0, 155.1, 145.0, 136.9, 134.4, 134.0, 131.6, 131.3, 130.5, 129.5, 129.5, 128.8, 126.7, 125.6 (q, J_{CF} = 3.8 Hz), 124.1 (q, J_{CF} = 3.9 Hz), 115.1, 82.5, 34.3, 31.6; HRMS (ESI-QTOF) calcd for $[C_{25}H_{24}F_3O_2]^+$ m/z 413.1723, found 413.1721.

*4-(1-(4-(tert-Butyl)phenoxy)-2-oxo-2-phenylethyl)benzonitrile (**5ab**).* Colorless oil (80.2 mg, 92%): IR (ATR) ν = 3060, 2959, 2229, 1695, 1605, 1509, 1447, 1363, 1231 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 7.6 Hz, 2H), 7.70 (d, J = 8.4 Hz, 2H), 7.67 (d, J = 8.0, 2H), 7.56 (t, J = 7.6 Hz, 1H), 7.43 (t, J = 7.6 Hz, 2H), 7.27 (d, J = 8.8 Hz, 2H), 6.86 (d, J = 8.4 Hz, 2H), 6.30 (s, 1H), 1.26 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.6, 154,9 145.2, 141.1, 134.2, 134.1, 132.8, 129.5, 128.9, 127.7, 126.7, 118.6, 115.1, 112.6, 82.5, 34.3, 31.6; HRMS (ESI-QTOF) calcd for $[C_{25}H_{24}NO_2]^+$ m/z 370.1802, found 370.1805.

*Methyl 3-(1-(4-methoxyphenyl)-2-oxo-2-phenylethoxy)benzoate (**5ac**).* Colorless oil (53.3 mg, 60%): IR (ATR) ν = 3066, 2951, 1718, 1694, 1585, 1510, 1486, 1445, 1282, 1249, 1216 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 7.6 Hz, 2H), 7.64−7.62 (m, 2H), 7.53 (t, J = 7.6 Hz, 1H), 7.48 (d, J = 8.4 Hz, 2H), 7.42 (t, J = 7.6 Hz, 2H), 7.30 (t, J = 7.6 Hz, 1H), 7.15−7.12 (m, 1H), 6.91 (d, J = 8.4 Hz, 2H), 6.42 (s, 1H), 3.86 (s, 3H), 3.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.5, 166.8, 160.2, 157.6, 134.7, 133.7, 131.7, 129.7, 129.3, 129.2, 128.8, 127.0, 123.0, 120.8, 116.6, 114.7, 82.3, 55.4, 52.3; HRMS (ESI-QTOF) calcd for $[C_{23}H_{21}O_5]^+$ m/z 377.1384, found 377.1383.

*Methyl 3-(1-(4-(ethoxycarbonyl)phenyl)-2-oxo-2-phenylethoxy)-benzoate (**5ad**).* Colorless oil (83.9 mg, 85%): IR (ATR) ν = 3069, 2952, 1715, 1706, 1587, 1486, 1445, 1367, 1271 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, J = 8.0 Hz, 2H), 8.01 (d, J = 7.6 Hz, 2H), 7.67−7.65 (m, 4H), 7.54 (t, J = 7.6 Hz, 1H), 7.42 (t, J = 7.6 Hz, 2H), 7.32 (t, J = 7.6 Hz, 1H), 7.16 (d, J = 8.4 Hz, 1H), 6.44 (s, 1H), 4.36 (q, J = 7.2 Hz, 2H), 3.88 (s, 3H), 1.37 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.2, 166.7, 166.2, 157.3, 139.9, 134.4, 134.0, 131.9, 131.1, 130.4, 129.9, 129.4, 128.9, 127.3, 123.4, 120.6, 116.5, 82.8, 61.3, 52.4, 14.5; HRMS (ESI-QTOF) calcd for $[C_{25}H_{23}O_6]^+$ m/z 419.1489, found 419.1482.

*1-(4-Fluorophenyl)-2-(4-methoxyphenyl)-2-phenoxyethanone (**5ae**).* White solid: mp 75.1−77.6 °C (67.5 mg, 85%); IR (ATR) ν = 3064, 2954, 1689, 1591, 1492, 1460, 1409, 1358, 1257, 1219 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.08 (dd, J = 6.0, 8.4 Hz, 2H), 7.47 (d, J = 8.4 Hz, 2H), 7.26−7.22 (m, 2H), 7.06 (t, J = 8.4 Hz, 2H), 6.97−6.90 (m, 5H), 6.26 (s, 1H), 3.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.8, 165.9 (d, J_{CF} = 254.4 Hz), 160.1, 157.6, 132.1 (d, J_{CF} = 9.3 Hz), 129.7, 128.8, 127.2, 121.9, 116.0, 115.8, 115.7, 114.6, 82.6, 55.4; HRMS (ESI-QTOF) calcd for $[C_{21}H_{18}FO_3]^+$ m/z 337.1234, found 337.1233.

*2-(3,4-Dimethoxyphenyl)-1-(4-fluorophenyl)-2-phenoxyethanone (**5af**).* White solid: mp 76.5−77.1 °C (80.4 mg, 93%); IR (ATR) ν = 3068, 2934, 1692, 1594, 1510, 1461, 1414, 1339, 1218 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.09 (dd, J = 5.6, 7.2 Hz, 2H), 7.26−7.23 (m, 2H), 7.10−7.04 (m, 4H), 6.98−6.93 (m, 3H), 6.87 (d, J = 8.4 Hz, 1H), 6.25 (s, 1H), 3.87 (s, 3H), 3.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.7, 157.6, 149.6, 132.2, 132.1, 129.8, 127.6, 122.0, 120.2, 116.1, 115.8, 115.76, 111.4, 110.2, 82.8, 56.1, 56.0; HRMS (ESI-QTOF) calcd for $[C_{22}H_{20}FO_4]^+$ m/z 367.1340, found 367.1347.

*4-(1-(4-Fluorophenoxy)-2-oxo-2-phenylethyl)benzonitrile (**5ag**).* Colorless oil (61.8 mg, 79%): IR (ATR) ν = 3068, 2924, 2229, 1694, 1593, 1490, 1409, 1217 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.07 (dd, J = 5.2, 8.4 Hz, 2H), 7.71 (d, J = 8.4 Hz, 2H), 7.68 (d, J = 8.4 Hz, 2H), 7.29−7.25 (m, 2H), 7.08 (t, J = 8.4 Hz, 2H), 7.00 (t, J = 7.2 Hz, 1H), 6.94 (d, J = 8.0 Hz, 2H), 6.27 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.1, 166.2 (d, J_{CF} = 255.7 Hz), 156.9, 140.7, 132.8, 132.4 (d, J_{CF} = 9.5 Hz), 130.0, 127.4, 122.6, 118.4, 116.2, 116.0, 115.5, 112.7, 82.8; HRMS (ESI-QTOF) calcd for $[C_{21}H_{15}FNO_2]^+$ m/z 332.1081, found 332.1085.

*1-(4-Fluorophenyl)-2-phenoxy-2-(3-(trifluoromethyl)phenyl)-ethanone (**5ah**).* White solid: mp 85.9−86.9 °C (76.9 mg, 87%); IR (ATR) ν = 3073, 2960, 1691, 1593, 1494, 1453, 1410, 1326, 1225 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.08 (t, J = 6.8 Hz, 2H), 7.87 (s, 1H), 7.76 (d, J = 7.2 Hz, 1H), 7.53 (d, J = 7.6 Hz, 1H), 7.52 (t, J = 7.6 Hz, 1H), 7.29−7.25 (m, 2H), 7.08 (t, J = 8.0 Hz, 2H), 7.01−6.95 (m, 3H), 6.29 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.6, 166.2 (d, J_{CF} = 255.2 Hz), 157.2, 136.6, 132.3 (d, J_{CF} = 9.4 Hz), 131.5 (d, J_{CF} = 32.6 Hz), 130.5 (d, J_{CF} = 3.1 Hz), 130.2, 130.0, 129.6, 125.8 (q, J_{CF} = 3.8 Hz), 123.7 (q, J_{CF} = 3.2 Hz), 122.4, 116.2, 116.0, 115.6, 82.8; HRMS (ESI-QTOF) calcd for $[C_{21}H_{15}F_4O_2]^+$ m/z 375.1003, found 375.1005.

*Ethyl 4-(2-(4-fluorophenyl)-2-oxo-1-phenoxyethyl)benzoate (**5ai**).* Colorless oil (80.4 mg, 90%): IR (ATR) ν = 3067, 2981, 1713, 1705, 1594, 1491, 1410, 1366, 1272, 1219 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.10−8.06 (m, 4H), 7.66 (d, J = 8.4 Hz, 2H), 7.28−7.24 (m, 2H), 7.07 (t, J = 8.4 Hz, 2H), 6.99 (d, J = 7.2 Hz, 1H), 6.95 (d, J = 8.4 Hz, 2H), 6.28 (s, 1H), 4.37 (q, J = 7.2 Hz, 2H), 1.38 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.6, 166.2, 157.3, 140.2, 132.4, 132.4, 131.0, 130.3, 129.9, 126.8, 122.3, 116.1, 115.9, 83.3, 61.3, 14.5; HRMS (ESI-QTOF) calcd for $[C_{23}H_{20}FO_4]^+$ m/z 379.1340, found 379.1343.

*Methyl 3-(2-(3,5-dimethoxyphenyl)-1-(4-methoxyphenyl)-2-oxoethoxy)-5-methoxybenzoate (**5aj**).* Yellow gum (92.5 mg, 84%): IR (ATR) ν = 3092, 2950, 1718, 1707, 1590, 1510, 1456, 1427, 1346, 1297, 1244, 1202, 1150 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 8.4 Hz, 2H), 7.22 (s, 1H), 7.18 (s, 1H), 7.14 (s, 2H), 6.90 (d, J = 8.4 Hz, 2H), 6.71 (s, 1H), 6.61 (s, 1H), 6.38 (s, 1H), 3.86 (s, 3H), 3.78 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.9, 166.7, 160.9, 160.8, 160.2, 158.6, 136.4, 132.2, 129.4, 126.9, 114.7, 109.0, 108.2, 107.3, 106.9, 106.0, 82.0, 55.7, 55.4, 52.4; HRMS (ESI-QTOF) calcd for $[C_{26}H_{27}O_8]^+$ m/z 467.1700, found 467.1706.

*Methyl 3-(2-(3,5-dimethoxyphenyl)-1-(4-(ethoxycarbonyl)-phenyl)-2-oxoethoxy)-5-methoxybenzoate (**5ak**).* Yellow gum (259.2 mg, 72%): IR (ATR) ν = 2935, 1714, 1590, 1455, 1428, 1347, 1274 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, J = 8.0 Hz, 2H), 7.64 (d, J = 8.0 Hz, 2H), 7.24 (s, 1H), 7.20 (s, 1H), 7.13 (s, 2H), 6.72 (s, 1H), 6.62 (s, 1H), 6.41 (s, 1H), 4.36 (q, J = 6.8 Hz, 2H), 3.87 (s, 3H), 3.79 (s, 3H), 3.78 (s, 6H), 1.37 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.6, 166.6, 166.1, 160.9, 158.3, 139.8, 136.0, 132.4, 131.1, 130.4, 127.4, 109.0, 108.5, 107.3, 107.1, 106.3, 82.5, 61.3, 55.8, 55.7, 52.5, 14.5; HRMS (ESI-QTOF) calcd for $[C_{28}H_{29}O_9]^+$ m/z 509.1806, found 509.1805.

*Ethyl 4-(1-(3,4-dimethoxyphenoxy)-2-oxo-2-phenylethyl)-benzoate (**5al**).* Yellowish gum (80.4 mg, 81%): IR (ATR) ν = 3062, 2932, 1713, 1704, 1596, 1508, 1447, 1413, 1366, 1272, 1226, 1194 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 8.0 Hz, 2H),

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8.01 (d, J = 8.4 Hz, 2H), 7.66 (d, J = 8.4 Hz, 2H), 7.54 (t, J = 7.6 Hz, 1H), 7.41 (t, J = 7.6 Hz, 2H), 6.69 (d, J = 8.8 Hz, 1H), 6.62 (d, J = 2.8 Hz, 1H), 6.37 (dd, J = 2.8, 8.8 Hz, 1H), 6.30 (s, 1H), 4.36 (q, J = 7.2 Hz, 2H), 3.81 (s, 3H), 3.80 (s, 3H), 1.37 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.1, 166.2, 151.9, 150.0, 144.5, 140.5, 134.5, 133.9, 130.9, 130.3, 129.4, 128.8, 127.1, 111.6, 105.3, 102.1, 83.5, 61.3, 56.4, 56.0, 14.5; HRMS (ESI-QTOF) calcd for $[C_{25}H_{25}O_6]^+$ m/z 421.1646, found 421.1643.

*2-(4-Chlorophenyl)-2-(3,4-dimethoxyphenoxy)-1-phenylethanone (**5am**).* Brown gum (58.7 mg, 65%): IR (ATR) ν = 3062, 2932, 1693, 1595, 1507, 1446, 1408, 1362, 1259, 1226, 1193 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 7.6 Hz, 2H), 7.56−7.50 (m, 3H), 7.40 (t, J = 7.6 Hz, 2H), 7.36 (d, J = 8.4 Hz, 2H), 6.68 (d, J = 8.8 Hz, 1H), 6.61 (d, J = 2.4 Hz, 1H), 6.35 (dd, J = 2.4, 8.4 Hz, 1H), 6.25 (s, 1H), 3.81 (s, 3H), 3.79 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.1, 151.9, 150.0, 144.4, 134.9, 134.5, 134.2, 133.9, 129.3, 128.8, 128.76, 111.5, 105.2, 102.1, 82.9, 56.4, 56.0; HRMS (ESI-QTOF) calcd for $[C_{22}H_{20}ClO_4]^+$ m/z 383.1045, found 383.1046.

*4-(1-(3,5-Dimethoxyphenoxy)-2-(3-methoxyphenyl)-2-oxoethyl)-benzonitrile (**5an**).* Brown gum (208.5 mg, 73%): IR (ATR) ν = 3072, 2935, 2228, 1694, 1592, 1458, 1427, 1319, 1262, 1202, 1146 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (s, 4H), 7.60 (d, J = 7.6 Hz, 1H), 7.50 (s, 1H), 7.34 (t, J = 8.0 Hz, 1H), 7.10 (d, J = 8.0 Hz, 1H), 6.33 (s, 1H), 6.11 (s, 3H), 3.81 (s, 3H), 3.72 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.9, 161.8, 160.0, 158.9, 140.7, 135.5, 132.8, 129.9, 127.9, 121.9, 120.7, 118.5, 113.7, 112.8, 94.6, 94.3, 82.0, 55.6, 55.5; HRMS (ESI-QTOF) calcd for $[C_{24}H_{22}NO_5]^+$ m/z 404.1492, found 404.1489.

*2-(3,5-Dimethoxyphenoxy)-2-(4-fluorophenyl)-1-(3-methoxyphenyl)ethanone (**5ao**).* Yellow gum (182.4 mg, 65%): IR (ATR) ν = 3074, 2937, 1694, 1591, 1508, 1458, 1426, 1322, 1264, 1225, 1202, 1144 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, J = 7.6 Hz, 1H), 7.55−7.51 (m, 3H), 7.32 (t, J = 8.0 Hz, 1H), 7.09−7.04 (m, 3H), 6.33 (s, 1H), 6.11 (d, J = 0.8 Hz, 2H), 6.08 (s, 1H), 3.80 (s, 3H), 3.71 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.3, 163.0 (d, J_{CF} = 246.7 Hz), 161.6, 159.6 (d, J_{CF} = 64.6 Hz), 135.8, 131.2 (d, J_{CF} = 3.2 Hz), 129.8, 129.5 (d, J_{CF} = 8.4 Hz), 121.7, 120.4, 116.3, 116.1, 113.5, 94.6, 94.1, 81.7, 55.5, 55.46; HRMS (ESI-QTOF) calcd for $[C_{23}H_{22}FO_5]^+$ m/z 397.1446, found 397.1445.

General Procedure for the Synthesis of 2, 6−16. A mixture of 2-arylated aryloxyketone **5** (0.1 mmol) and catalyst in toluene (3.0 mL) was heated at 130 °C. The reaction mixture was concentrated under reduced pressure to give the crude residue, which was purified by silica gel column chromatography (hexane:ethyl acetate:dichloromethane) to afford **2**, **6−16**.

*Methyl 3-(3,5-dimethoxyphenyl)-6-methoxy-2-(4-methoxyphenyl)benzofuran-4-carboxylate (**2**).*[7] Brown solid: mp 139.9−143.5 °C (23.8 mg, 53%); IR (ATR) ν = 3097, 2929, 1714, 1621, 1595, 1572, 1510, 1460, 1322, 1242 cm^{-1}; ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.40 (s, 1H), 7.25 (d, J = 8.0 Hz, 2H), 7.19 (s, 1H), 7.09 (d, J = 8.0 Hz, 2H), 6.67 (s, 2H), 6.41 (s, 1H), 3.95 (s, 3H), 3.87 (s, 3H), 3.64 (s, 6H), 3.16 (s, 3H); ^{13}C NMR (100 MHz, Acetone-d_6) δ 167.8, 161.8, 160.4, 158.8, 156.2, 152.0, 133.0, 132.0, 127.3, 127.2, 122.2, 118.8, 115.1, 114.0, 105.3, 101.6, 99.7, 56.5, 55.8, 55.6, 51.9; HRMS (ESI-QTOF) calcd for $[C_{26}H_{25}O_7]^+$ m/z 449.1595, found 449.1599.

*2-(4-Chlorophenyl)-6-methoxy-3-(4-methoxyphenyl)benzofuran (**6**).* White solid: mp 114.7−119.6 °C (lit. 117 °C)[20] (34.3 mg, 94%); IR (ATR) ν = 3060, 2922, 1585, 1510, 1485, 1453, 1399, 1371, 1343, 1270, 1244 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, J = 8.0 Hz, 2H), 7.39 (d, J = 8.0 Hz, 2H), 7.33 (d, J = 8.8 Hz, 1H), 7.26 (d, J = 7.6 Hz, 2H), 7.07 (s, 1H), 7.00 (d, J = 8.0 Hz, 2H), 6.87 (d, J = 8.8 Hz, 1H), 3.88 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4, 158.7, 155.1, 148.4, 133.6, 130.9, 129.7, 128.8, 127.7, 124.8, 123.9, 120.5, 117.8, 114.7, 112.2, 95.8, 55.9, 55.5; HRMS (ESI-QTOF) calcd for $[C_{22}H_{18}ClO_3]^+$ m/z 365.0939, found 365.0938.

*3-(4-Methoxyphenyl)-5-phenyl-2-(3,4,5-trimethoxyphenyl)-benzofuran (**7**).* Yellow solid: mp 170.0−171.7 °C (19.6 mg, 42%); IR (ATR) ν = 2928, 2830, 1602, 1579, 1511, 1456, 1408, 1382, 1301, 1232, 1171 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66−7.65 (m, 3H), 7.61−7.58 (m, 3H), 7.55−7.53 (m, 1H), 7.44 (t, J = 7.6 Hz, 2H), 7.33 (t, J = 7.2 Hz, 1H), 6.89 (d, J = 8.4 Hz, 2H), 6.73 (s, 2H), 3.96 (s, 3H), 3.84 (s, 3H), 3.81 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.0, 153.9, 153.5, 151.4, 141.8, 136.8, 131.1, 128.9, 128.6, 127.6, 127.0, 124.2, 123.2, 118.3, 116.3, 114.1, 111.3, 106.9, 61.2, 56.4, 55.5; HRMS (ESI-QTOF) calcd for $[C_{30}H_{27}O_5]^+$ m/z 467.1853, found 467.1858.

*4-(5-Chloro-3-phenylbenzofuran-2-yl)benzonitrile (**8**).* Yellow solid: mp 213.2−215.4 °C (14.2 mg, 43%); IR (ATR) ν = 3063, 2921, 2224, 1603, 1443, 1258 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 8.4 Hz, 2H), 7.59 (d, J = 8.4 Hz, 2H), 7.54−7.48 (m, 4H), 7.45−7.44 (m, 3H), 7.34 (dd, J = 2.0, 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.7, 149.6, 134.5, 132.4, 131.5, 131.4, 129.62, 129.60, 129.3, 128.8, 127.2, 126.2, 120.3, 120.2, 118.8, 112.5, 111.9; HRMS (ESI-QTOF) calcd for $[C_{21}H_{13}ClNO]^+$ m/z 330.0680, found 330.0686.

*5-(tert-Butyl)-2-(4-methoxyphenyl)-3-phenylbenzofuran (**9**).* White solid: mp 125.7−126.8 °C (22.5 mg, 63%); IR (ATR) ν = 3061, 2953, 1608, 1565, 1511, 1471, 1363, 1245, 1174 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J = 7.6 Hz, 2H), 7.48−7.38 (m, 5H), 7.32−7.24 (m, 3H), 7.02 (d, J = 8.4 Hz, 2H), 3.89 (s, 3H), 1.36 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2, 152.3, 150.6, 146.2, 131.1, 131.07, 130.2, 128.5, 128.2, 127.0, 125.3, 122.8, 117.5, 116.1, 114.6, 110.5, 55.4, 34.9, 32.0; HRMS (ESI-QTOF) calcd for $[C_{25}H_{25}O_2]^+$ m/z 357.1849, found 357.1847.

*5-(tert-Butyl)-2-(3,4-dimethoxyphenyl)-3-phenylbenzofuran (**10**).* White solid: mp 118.1−119.2 °C (31.7 mg, 82%); IR (ATR) ν = 3057, 2948, 1574, 1512, 1462, 1441, 1407, 1371, 1311, 1248, 1227 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, J = 6.8 Hz, 2H), 7.48−7.47 (m, 2H), 7.40 (d, J = 8.8 Hz, 1H), 7.33−7.25 (m, 3H), 7.08 (d, J = 8.0 Hz, 1H), 7.01−6.99 (m, 2H), 3.97 (s, 3H), 3.81 (s, 3H), 1.36 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.3, 150.7, 149.4, 148.6, 146.2, 131.0, 130.1, 128.5, 128.3, 127.0, 125.6, 122.8, 122.2, 117.6, 116.1, 113.0, 111.8, 110.6, 56.0, 35.0, 32.0; HRMS (ESI-QTOF) calcd for $[C_{26}H_{27}O_3]^+$ m/z 387.1955, found 387.1949.

*5-(tert-Butyl)-3-phenyl-2-(3-(trifluoromethyl)phenyl)benzofuran (**11**).* White solid: mp 97.6−99.3 °C (30.0 mg, 76%); IR (ATR) ν = 3066, 2959, 1612, 1451, 1365, 1323, 1279, 1243, 1205, 1163, 1121 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.73 (d, J = 8.0 Hz, 1H), 7.51−7.43 (m, 9H), 7.37 (t, J = 7.6 Hz, 1H), 1.36 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.5, 149.1, 146.6, 132.5, 131.8, 129.8, 129.7, 129.4, 129.0, 128.2, 124.7 (q, J_{CF} = 3.7 Hz), 123.7 (q, J_{CF} = 4.0 Hz), 123.5, 119.3, 116.3, 110.7, 35.0, 32.0; HRMS (ESI-QTOF) calcd for $[C_{25}H_{22}F_3O]^+$ m/z 395.1617, found 395.1615.

*Methyl 3-(3,5-dimethoxyphenyl)-2-(4-(ethoxycarbonyl)phenyl)-6-methoxybenzofuran-4-carboxylate (**12**).*[7a] Yellow solid: mp 125.6−127.7 °C (25.0 mg, 51%); IR (ATR) ν = 3084, 2925, 1720, 1713, 1594, 1493, 1457, 1423, 1376, 1349, 1313, 1272, 1192 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J = 8.0 Hz, 2H), 7.61 (d, J = 8.0 Hz, 2H), 7.26 (s, 1H), 7.24 (s, 1H), 6.52 (s, 1H), 6.49 (s, 2H), 4.36 (q, J = 7.2 Hz, 2H), 3.92 (s, 3H), 3.77 (s, 6H), 3.25 (s, 3H), 1.38 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8, 166.3, 161.4, 158.1, 155.8, 150.3, 136.0, 134.5, 129.7, 126.4, 126.2, 121.2, 119.4, 113.3, 107.4, 100.5, 99.5, 61.2, 56.2, 55.6, 51.7, 14.5; HRMS (ESI-QTOF) calcd for $[C_{28}H_{27}O_8]^+$ m/z 491.1700, found 491.1703.

*Ethyl 4-(5,6-dimethoxy-3-phenylbenzofuran-2-yl)benzoate (**13**).* White solid: mp 135.4−137.5 °C (28.2 mg, 70%); IR (ATR) ν = 3076, 2925, 1711, 1605, 1476, 1307, 1266 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J = 8.4 Hz, 2H), 7.64 (d, J = 8.8 Hz, 2H), 7.50−7.45 (m, 5H), 7.13 (s, 1H), 6.86 (s, 1H), 4.36 (q, J = 7.2 Hz, 2H), 3.98 (s, 3H), 3.87 (s, 3H), 1.38 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 149.2, 149.2, 148.5, 147.2, 135.1, 132.8, 129.8, 129.3, 129.2, 128.1, 125.9, 122.2, 120.0, 101.3, 95.2, 61.1, 56.54, 56.47, 14.5; HRMS (ESI-QTOF) calcd for $[C_{25}H_{23}O_5]^+$ m/z 403.1540, found 403.1545.

*2-(4-Chlorophenyl)-5,6-dimethoxy-3-phenylbenzofuran (**14**).* Orange solid: mp 154.6−155.9 °C (21.9 mg, 60%); IR (ATR) ν = 3049, 2928, 1599, 1475, 1307 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52−7.43 (m, 7H), 7.26−7.24 (m, 2H), 7.11 (s, 1H), 6.87 (s, 1H), 3.97 (s, 3H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.9, 147.1, 133.6, 133.0, 131.2, 129.8, 129.6, 129.3, 128.8, 128.0, 127.7, 126.6,

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122.2, 118.4, 101.3, 95.2, 56.6, 56.5; HRMS (ESI-QTOF) calcd for $[C_{22}H_{18}ClO_3]^+$ m/z 365.0939, found 365.0937.

*4-(4,6-Dimethoxy-3-(3-methoxyphenyl)benzofuran-2-yl)-benzonitrile (**15**).* Yellow solid: mp 201.9−202.8 °C (25.8 mg, 67%); IR (ATR) ν = 3070, 2960, 2217, 1594, 1572, 1498, 1457, 1426, 1366, 1319, 1278, 1235, 1211 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, J = 8.4 Hz, 2H), 7.50 (d, J = 8.4 Hz, 2H), 7.33 (t, J = 7.6 Hz, 1H), 7.01−6.93 (m, 3H), 6.70 (s, 1H), 6.30 (s, 1H), 3.89 (s, 3H), 3.81 (s, 3H), 3.68 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.4, 159.6, 156.3, 155.3, 146.4, 135.3, 134.4, 132.2, 129.5, 126.3, 122.7, 120.7, 119.1, 115.8, 113.8, 113.2, 110.3, 95.0, 87.9, 55.9, 55.6, 55.4; HRMS (ESI-QTOF) calcd for $[C_{24}H_{20}NO_4]^+$ m/z 386.1387, found 386.1388.

*2-(4-Fluorophenyl)-4,6-dimethoxy-3-(3-methoxyphenyl)-benzofuran (**16**).* Brown gum (28.4 mg, 75%): IR (ATR) ν = 3068, 2960, 1595, 1572, 1496, 1426, 1366, 1319, 1279, 1235, 1210 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.45 (dd, J = 5.6, 8.0 Hz, 2H), 7.29 (t, J = 8.0 Hz, 1H), 7.03−7.01 (m, 2H), 6.96−6.91 (m, 3H), 6.69 (s, 1H), 6.30 (s, 1H), 3.87 (s, 3H), 3.79 (s, 3H), 3.68 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.2 (d, J_{CF} = 246.6 Hz), 159.4 (d, J_{CF} = 4.3 Hz), 155.9, 154.9, 148.0, 134.9, 129.2, 128.4 (d, J_{CF} = 8.0 Hz), 127.3 (d, J_{CF} = 3.4 Hz), 123.2, 117.1, 116.0, 115.6, 115.3, 113.5, 113.0, 94.8, 88.0, 55.9, 55.6, 55.4; HRMS (ESI-QTOF) calcd for $[C_{23}H_{20}FO_4]^+$ m/z 379.1340, found 379.1343.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^1H and ^{13}C NMR spectra of compounds **2**, **4**, **5**−**16**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ DEDICATION

†This paper is dedicated to the memory of my friend, Dr. Junwon Kim, who passed away on April 2013.

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